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Amendments to the Specification:

Please replace paragraph [0003] of the published application with the following amended paragraph:

Alzheimer's Disease (AD) represents one of the great unsolved medical needs confronting society during this millennium. Despite considerable work during the past quarter century, no medicines exist that attack the underlying pathophysiology of the disease. One of the cardinal features of AD is deposition of plaques comprised of aggregated beta-amyloid peptides (Aβ) in the brain, particularly in regions associated with cognition and memory. Selkoe, *Annu. Rev. Neurosci.*, 17, 489-517 (1994). Overproduction of Aβ, which appears to be directly neurotoxic, can be detected at the earliest stages of AD and, in fact, before cognitive dysfunction is detectable. [[AD]]Aβ is produced from its precursor protein, APP, by proteolytic processing at its N and C termini by β- and γ-secretase enzymes, respectively. Mutations in APP, presenilin-1, or presenilin-2 genes result in over-production of Aβ1-42 peptide and cause early onset, familial AD. The identity of the β- and γ-secretases have been studied since 1984, and in 1999 the elusive N-terminal β-site APP cleaving enzyme (BACE-1) was reported. Yan, *et al.*, *Nature*, 402, 533-537 (1999). It remains possible that there are additional proteases with [[≈]]β-secretase activity.

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Please replace paragraph [0046] of the published application with the following amended paragraph:

Some transgenic animals of the invention have both an inactivation of one or both alleles of BACE-1 and a second transgene that confers an additional phenotype related to Alzheimer's,